Title: It's All in The Tissue—A Rare Case of Acute Cardiogenic Shock

A 53 year-old female with a history of hypothyroidism (Hashimoto's) presented to the emergency department with a two-week history of worsening shortness of breath and abdominal discomfort. She denied chest pain, palpitations, syncope, or fevers. She did endorse resting dyspnea and orthopnea. Her vitals on presentation: heart rate of 120 bpm (regular rhythm), blood pressure 87/69 mmHg, respiratory rate of 22 breaths/min, oxygen saturation of 96% on 3L supplemental oxygen. Her exam was notable for elevated JVP, 3/6 holosystolic murmur at the left fifth intercostal space, and bilateral inspiratory crackles. Her hands and feet were cool to touch with 1+ pitting edema in both lower extremities, from mid-shin to feet.

Laboratory analysis revealed normal kidney function, transaminitis (AST: 850 u/L, ALT: 960 u/L), white blood cell count of 21,000 u/L, elevated lactic acid at 3.1 mmol/L, Troponin-T 3.1 ng/L and C-Reactive Protein 86 mg/L. Thyroid stimulating hormone and free thyroxine levels were within normal limits. EKG showed sinus rhythm, low-voltage across precordium, 2 mm ST-segment elevations in V1-V2, anterolateral ST depressions and inferior T-wave inversions (Figure 1). Chest film revealed normal cardiac silhouette size and moderately sized bilateral pleural effusions. Echocardiogram showed normal left ventricle (LV) cavity size, LV ejection fraction of 25%, apical hypokinesis, mildly dilated right ventricle (RV) with moderately reduced function. Mild mitral and tricuspid regurgitation were both noted.

The differential diagnosis for this acute heart failure syndrome included ischemic disease, myocarditis and cardiomyopathy secondary to sepsis. With the marked leukocytosis and elevated inflammatory markers, myocarditis was suspected, with fulminant lymphocytic myocarditis and giant cell myocarditis believed to be most likely given the rapid presentation and hemodynamic compromise. Other causes of myocarditis, such as sarcoidosis, were less likely as they tend to have a more subacute presentation. The low-voltage complexes on the EKG supported an infiltrative process. Amyloidosis was less likely given the lack of ventricular hypertrophy or significant atrial enlargement. A cardiomyopathy related to hypothyroidism was ruled out by the normal thyroid studies. The EKG was also not suggestive of alternative causes of cardiomyopathy such as arrhythmogenic right ventricular dysplasia.

Given clinical evidence of cardiogenic shock, immediate coronary angiography was performed and demonstrated no obstructive coronary artery disease. Subsequent right heart catheterization was performed and showed: right atrial pressure 19 mmHg, right ventricular pressure 33/15 mmHg, pulmonary artery pressure of 33/15/25 mmHg, pulmonary capillary wedge pressure 25 mmHg, pulmonary artery saturation 47%, estimated Fick cardiac index 1.5 L/min/m^2. Intra-aortic balloon pump was inserted for stabilization. An endomyocardial biopsy was performed due to the fulminant presentation requiring mechanical support. In the hour following cardiac catheterization, she developed ventricular arrhythmias and worsening hypotension which prompted interdisciplinary discussion between cardiac surgery and the advanced heart failure team, with a joint decision to upgrade her support to CentriMag™ (Abbott) biventricular assist devices. Echocardiography showed severe biventricular dysfunction and the pulmonary artery pulsatility index (PA systolic – PA diastolic pressures)/(RA Pressure) was calculated at 0.95, indicating severe right ventricular dysfunction[1], which supported the decision to pursue biventricular mechanical support. The pathology from the

endomyocardial biopsy (Figure 2) revealed diffuse mononuclear lymphocytic infiltrate, myocardial necrosis, and multi-nucleated giant cells without granulomatous formation, confirming the diagnosis of giant cell myocarditis.

Giant cell myocarditis is a rare cause of cardiomyopathy with an estimated incidence of 0.13 cases per 100,000 persons[2]. The typical manifestation is congestive heart failure, and may be accompanied by new-onset high-degree heart block or ventricular arrhythmias. Giant cell myocarditis presents fulminantly, with an estimated rate of death or cardiac transplantation approaching 90% in some case series[3]. The pathophysiology of Giant cell myocarditis is not well understood and is thought to be mediated by a T-cell mediated autoimmune process. Specifically, anti-myosin antibodies activate macrophages and stimulate the production of tumor necrosis factor and nitric oxide synthase, leading to apoptosis and myocardial necrosis[4]. Confirming the diagnosis of giant cell myocarditis by endomyocardial biopsy is critical because this disease responds to immunosuppression. Observational data has demonstrated improved survival with immunosuppressive therapy in giant cell myocarditis[5, 6]. Our patient received a combination a high-dose corticosteroids and tacrolimus to suppress T-cell activity.

Our patient's clinical status improved over two weeks on biventricular support. Arterial waveform pulsatility was seen, suggesting myocardial recovery. A decision was made to perform a BiVAD speed "turn-down" study to assess for myocardial recovery on minimal support. Under simultaneous echocardiographic and invasive hemodynamic guidance, assist device speeds were gradually reduced to achieve one-liter of flow. With minimal mechanical circulatory support, LVEF was estimated to be 45%, LV end-diastolic diameter was 4.5 cm, and RV function was normal. Filling pressures and cardiac index remained normal during the "turn-down" study (Figure 3A), and the multidisciplinary team decided to proceed with device explanation. The patient was successfully transitioned to medical therapy for heart failure along with continued long-term immunosuppression with Tacrolimus and tapering doses of steroids. On follow-up cardiac MRI eight months later, LVEF and RVEF were both estimated to be > 55%, and no signs of active inflammation were present.

This case demonstrates the importance of early biventricular support instead of sole LV unloading strategies in acute cardiomyopathies with global involvement. We have proposed an algorithm for unexplained, new-onset cardiogenic shock as shown (Figure 3B). Stepwise assessment of the patient including recognition of shock etiology, deciding when to upgrade support for progression of disease, assessing for recovery, and knowing if durable heart replacement therapies are needed are important aspects in the approach to cardiogenic shock. This case further underscores the importance of timely endomyocardial biopsy in unexplained acute cardiomyopathies, as it can be critical in guiding therapy for variants of myocarditis, such as GCM, which are responsive to immunosuppression.

References:

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